REMARKS

Claim Rejections Under 35 U.S.C. § 112, first paragraph

All pending claims clearly comply with the written description requirement. The language presently used in the claims is original language and no evidence has been presented that this language is vague or ambiguous or that the language encompasses subject matter beyond the invention provided. It is alleged that the specification does not describe what is meant by the various definitions for the variables A, B, R_y, R_z and R_x. Reference is made to the phrase "substituted moiety of up to 40 carbon atoms used to define variable 'A'." This is a partial definition of the variable "A" and it describes a size limit for these moieties. Similarly, variables B, R_y, R_z and R_x are defined as organic moieties and given size limits described by the number of carbon atoms therein. While the definitions provided are broad, no evidence has been presented that they are ambiguous or that they encompass subject matter beyond the invention provided. The detailed disclosure and examples give examples of each of these variables which provide further guidance as to the meaning of these variables.

The specification identifies publications which demonstrate that the inhibition of the raf kinase signal pathway a) leads to the reversion of transformed cells to the normal growth phenotype (see Daum et al., *Trends Biochem. Sci.*, 1994, 19, 474-80; Fridman et al., *J. Biol. Chem.*, 1994, 269, 30105-8), b) blocks cell proliferation in membrane-associated oncogenes (Kolch et al., *Nature*, 1991, 349, 426-28), c) is correlated *in vitro* and *in vivo* with the inhibition of a growth of a variety of tumor types (Monia et al., *Nat. Med.*, 1996, 2, 668-75). Based on this disclosure and others within the specification as well as the conventional knowledge of skilled artisans, the pending claims are not ambiguous in defining a treatment of cancerous cell growth mediated by raf kinase or the treatment of solid cancers or the

treatment of carcinomas, myeloid disorders or adenomas. With the compounds demonstrating raf kinase inhibition and the raf kinase signal pathway being associated with various conditions including treatment of solid cancers, this language does not encompass subject matter beyond the invention provided and one skilled in the art would clearly understand and recognize the scope of these terms in defining the conditions to be treated with the compounds of this invention.

The language employed in the pending claims is not inconsistent with the holdings in the *Regents of University of California v. Ely Lilly & Co.* and *Enzo Biochem, Inc. v. Gen-Probe* cited by the Examiner. No evidence has been presented that the method claims are imprecise in defining the treatment of a raf mediated disorders and the holding in *Enzo* recognizes that functional characteristics can provide a complete disclosure where there is a known or disclosed correlation between function and structure. As described in the specification, the correlation of the inhibition of the raf kinase signal pathway and certain diseases was known at the time of the invention.

Enablement

All pending claims clearly satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. The examiner has reviewed the factors mentioned in *In re Wands* but provides no evidence to support the rejection. The examiner alleges that claims are very broad but provides no evidence or suggestion that any of the compounds claimed cannot perform the intended function. The Examiner alleges the specification provides no guidance in treating cancers. However, dosages and methods of administration are described on pages 10–14. In addition, the Examiner alleges that one skilled in the art would be burdened

with undue experimentation to determine if the generic group of compounds of Formula (I) would be enabled. The nature of this experimentation is not identified.

The specification provides a number of publications which have correlated the inhibition of raf kinase with the inhibition of the growth of a variety of tumor types (Monia et al.), correlated the inhibition of raf expression with blocking cell proliferation (Kolch et al.) or correlated the inhibition of the raf kinase pathway with the reversion of transformed cells to the normal growth phenotype (Daum et al., Fridman et al).

No evidence has been presented to refute the findings or conclusions made in these publications. In addition, no evidence has been presented that any compounds of this invention, as inhibitors of raf kinase, would not be effective in treating the cancers identified.

The specification provides ample guidance as to how to prepare pharmaceutical compositions with the compounds of this invention and how to administer these compositions in the treatment of cancers. See, e.g., pages 10-14. The specification also provides dosage ranges for the various methods of administration (see page 13). Given the extent of the disclosure provided, it would at most involve routine experimentation if any at all, for one of ordinary skill in the art to treat any one of the recited cancers with a compound of this invention.

Even absent the specification disclosures discussed above, the rejection is clearly deficient in general under controlling case law. The courts have placed the burden upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971) (holding that how an enablement teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance.) The disclosure must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to

doubt the objective truth of the statements contained therein. See *In re Marzocchi*, supra. No such evidence or reason for doubting Applicants' disclosure has been provided. Only general statements and conclusions are made.

Additionally, "the [enablement] requirement is satisfied if, given what they [, those of ordinary skill in the art,] already know, the specification teaches those in the art enough that they can make and use the claimed invention without 'undue experimentation'." See *Amgen v Hoechst Marion Roussel*, 314 F.2d 1313, 65 USPQ2d 1385 (Fed. Cir. 2003). Using the claimed compounds would be routine for those of ordinary skill in the art in view of applicant's disclosure. Explicitly providing dedicated assays for each form of cancer is not necessary to enable the methods claimed. See, for example, *In re Howarth,* 654 F.2d 105, 210 U.S.P.Q. 689 (CCPA 1981) ("An inventor need not ... explain every detail since he is speaking to those skilled in the art."); *In re Gay*, 309 F.2d 769, 774, 135 U.S.P.Q. 311 (CCPA 1962) ("Not every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be.")

There is no requirement that an applicant provide any working examples relating to the treatment of every claimed disease to satisfy the statute. See, for example, *In re Angstadt*, 537 F.2d at 502-03, 190 USPQ 214 (CCPA 1976) (deciding that applicants "are *not* required to disclose *every* species encompassed by their claims even in an unpredictable art"); *Utter v Higara*, 845 F.2d at 998-99, 6 USPQ2d 1714 (Fed. Cir. 1988) (holding that a specification may, within the meaning of Section 112, Para. 1, enable a broadly claimed invention without describing all species that claim encompasses). Instead, as discussed earlier, there is no requirement for any examples. See, for example, *Marzocchi*, supra, stating that how "an enabling teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance." The MPEP also agrees by stating that "compliance with

the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." See MPEP § 2164.02.

The PTO has failed to meet its burden of establishing that the disclosure does not enable one skilled in the art to make and use the compounds recited in the claims. Instead of relying on proper probative evidence, the rejection is improperly based on bare allegations and conclusions. No evidence has been presented which would demonstrate that the guidance provided by the specification is inadequate to enable the use of the claimed compounds without undue experimentation.

As discussed in Wands, cited by the Examiner, "considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." Moreover, with respect to pharmaceutical inventions, an applicant is not required to test the claimed compounds in their final use (rigorous planned and executed clinical trials..." per the Examiner). The Federal Circuit in *In re Brana*, 51 F.3d 1560, 34 USPQ 1436 (Fed. Cir. 1995), stated that:

> usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful can be well before it is ready to be administered to humans. If the courts were to require Phase II testing in order to prove utility for pharmaceutical inventions, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas.

Here, the specification provides more than it needs to, e.g., *in vitro* raf kinase assays (and IC_{50} data) and *in vivo* assays (see pages 94 and 96). In similar fashion, one of ordinary skill in the art by performing the same or similar tests, can, by routine experimentation,

determine the activity levels of each of the claimed compounds in treating various cancers. This is absolutely routine in the field.

Thus, appellants have provided more than adequate guidance (and examples) to enable the claimed invention.

For the reasons discussed above, Applicants submit that claims 74, 80, 81, 87 and 93 meet the requirements of 35 U.S.C. § 112, first paragraph.

Obviousness-Type Double Patenting

These provisional rejections will be addressed once the claims herein are otherwise in condition for allowance.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

Richard J. Traverso, Reg. No. 30,595
Attorney/Agent for Applicants

MILLEN, WHITE, ZELANO &
BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: **BAYER-0024-A**

Date: **September 23, 2004**

(RJT/dlm) K:\Bayer\24A\Reply to 3-23-04 OA.doc